Preoperative KOOS and SF36 are associated with the development of symptomatic knee osteoarthritis at 7 years following ACL reconstruction

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Abstract

Background—Anterior cruciate ligament (ACL) tears are associated with the development of knee osteoarthritis in many patients despite ACL reconstruction surgery. However, little evidence is available to determine which patients will develop symptomatic knee osteoarthritis.

Objective—To determine if preoperative outcome measures were associated with the future development of a symptomatic knee 7 years following ACL reconstruction. A secondary goal was to examine the relationship between imaging evidence of knee osteoarthritis and development of knee pain.

Study Design—Case control study

Methods—Prospectively collected data from 72 subjects with 7 year follow-up after unilateral ACL reconstruction were reviewed. Subjects were divided into symptomatic and asymptomatic groups based on the previously defined Knee Osteoarthritis Outcome Score (KOOS) Pain score of 72. Demographic variables and preoperative KOOS and SF36 scores were compared between groups. Radiographic and magnetic resonance imaging data were used to evaluate differences in joint space width, OARSI radiographic score, and the Whole-Organ Magnetic Resonance Imaging (WORM) Score between groups. Univariate and multivariate analyses were performed to identify potential predictors of pain at 7 year follow-up. Wilcoxon Sum Rank and T-tests were used to compare imaging findings between the symptomatic and asymptomatic subjects at 7 years.

Results—Based on final KOOS Pain score, 7 of the 72 subjects available at 7 year follow-up formed the symptomatic group. No differences were found between groups in regards to demographic variables or intraoperative findings. In multivariate analysis, lower pre-operative KOOS Sports & Recreation (p=0.005) and lower pre-operative SF36 Mental Health (p=0.025)

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scores were found to be associated with a painful knee at 7 years, with increased odds of 82% and 68% per 10 unit decrease respectively. The WORM score at 7 years showed evidence of osteoarthritic changes in the symptomatic group compared to the asymptomatic group (p=.047). However, there were no significant differences in the OARSI radiographic score (p=.051) or joint space width (p=.488) between groups.

Conclusions—Lower preoperative KOOS and SF36 scores were associated with those patients who developed symptomatic knee osteoarthritis 7 years following ACL reconstruction.

Keywords

Anterior cruciate ligament; Reconstruction; Osteoarthritis; KOOS; SF36

INTRODUCTION

Anterior cruciate ligament (ACL) reconstruction has proven to be successful in restoring knee stability following an ACL tear in most patients.[8,19] However, athletes who suffer an ACL tear remain at an elevated risk of knee osteoarthritis despite ACL reconstruction. [1,7,18,26] As would be anticipated, the development of knee osteoarthritis following ACL reconstruction has been shown to correlate with worse patient reported outcomes.[7]

Several studies have attempted to identify risk factors for osteoarthritis following ACL reconstruction.[7,18,21,26] However, the evidence is limited by the heterogeneous patient populations, variable methods of measuring and reporting the data, and the need for longer term follow-up to confirm radiographic evidence of knee osteoarthritis.[4] Furthermore, little evidence is available to determine which patients are at risk for developing symptoms associated with knee osteoarthritis following ACL reconstruction.

The Knee Osteoarthritis Outcome Score (KOOS) is a patient reported outcome consisting of five scores that has been validated for measuring outcomes following knee injury.[9,27] The KOOS Pain score has been shown to correlate with structural changes of the knee associated with knee osteoarthritis.[17,23] In addition, this score has been previously used as a marker for significant knee pain and osteoarthritis following ACL reconstruction.[32]

Previous studies have examined the relationship between baseline patient variables and patient reported outcomes on KOOS.[5,10,28–30] However, little data exist to show a relationship between baseline patient-reported outcome measures and the future development of symptomatic knee osteoarthritis after ACL reconstruction. The purpose of this study was to determine if preoperative patient reported outcome measures were associated with the development of a symptomatic knee 7 years following ACL reconstruction. A secondary aim of the study was to determine if subjects with knee pain at 7 years have structural evidence of knee osteoarthritis. Our hypothesis was that the preoperative patient reported outcome measures will be associated with those patients who present with a painful knee at 7 year follow-up. Our secondary hypothesis was that patients with symptomatic knees following ACL reconstruction will have structural evidence of knee osteoarthritis on imaging studies.

MATERIALS & METHODS

Study Design

A case control study was performed using prospectively collected data as part of a previously published randomized controlled study [NCT00434837]. The analyses presented here are unique and address different hypotheses than the original study. The investigation was approved by the Institutional Review Board and all subjects provided informed consent. Patients were recruited from the clinics of three surgeons over a three year period. Inclusion criteria included the age range of 15 to 50 years, Tegner activity score 2, and candidates for patellar tendon or hamstring autograft reconstruction. Subjects were excluded if they had a previous injury to either knee, evidence of osteoarthritis in either knee on preoperative radiographs, disease predisposing them to articular cartilage damage, moderate size fissures or lesions of the articular cartilage (ICRS Grade 2, 3, or 4),[13] tears of the meniscus involving greater than the central third of the meniscus, or increased laxity (>Grade I) in the MCL, LCL, or PCL relative to the contralateral knee. ACL reconstruction was performed with either a patellar tendon or four-strand hamstring autograft, the selection of which was based on surgeon and/or patient preference. In the original study subjects were randomly assigned to high tension or low tension ACL reconstruction. However, no differences in outcomes were found at 3 years and only the KOOS Sports/Recreation score was statistically different between groups at 7 years. Therefore the groups were combined for the current analysis.[2,15]

Preoperative Data Set

Baseline data including demographics, time to surgery, graft type, graft tension, knee laxity on KT-1000 and the presence of cartilage or meniscal injuries identified at the time of ACL reconstruction were collected. In addition, patient reported outcome measures included the KOOS and SF36V2.[27,31] The KOOS evaluated five domains: 1. Knee related Quality of Life (QOL); 2. Sports and Recreation (Sports/Rec); 3. Activities of Daily Living (ADL); 4. Symptoms; and 5. Pain. The instrument has been previously validated in subjects after ACL reconstruction.[27] The SF36 is a self-report measure of functional health and wellbeing.[31] The questionnaire includes assessments of bodily pain (BP), general mental health (MH), limitations in usual role activities due to emotional problems (RE), limitations in usual role activities due to physical problems (RP), limitations in physical function (PF), limitations in social activities due to physical or emotional problems (SF), and vitality (V).

7 Year Post-op Data Set

The KOOS and SF36 data were also obtained at the 7 year follow-up. In addition, lateral and posterior-anterior radiographs of both the operative and contralateral knee were obtained and scored by a musculoskeletal radiologist, blinded to group and clinical outcomes. Medial joint space width was measured at the middle of the medial compartment on standardized semi-flexed posterior-anterior radiographs using a validated computer algorithm.[12] The modified Osteoarthritis Research Society International (OARSI) radiographic score was used to quantify osteoarthritic changes of the knee.[3] The measure included grading of osteophyte formation, joint space narrowing, as well as sclerosis, attrition, and ligament calcification yielding a score between 0 and 47. Magnetic resonance imaging was also performed for both knees. The semi-quantitative Whole Organ Magnetic Resonance Imaging

Score (WORMS) was used to assess the overall status of structural damage associated with knee osteoarthritis.[25]

Determination of Patients with Arthrosis

The KOOS Pain score was used to identify subjects with significant knee pain at 7 years. Consistent with previously published outcome studies, a cutoff of two standard deviations below the mean based on athletic patients with a history of knee ligament injury was used.[32] Using this mean value, subjects with a KOOS Pain score 72 at 7 years comprised the symptomatic group for comparison with the asymptomatic group with KOOS Pain scores >72.[32]

Statistical analysis

Seven year changes in KOOS and SF36 scores were evaluated based on paired t-tests. Two sample t-tests were used to compare subjects classified at 7 years as symptomatic and asymptomatic on baseline measures of KOOS, SF36 and other characteristics. Categorical baseline measures were compared between groups using chi square tests. Univariate logistic regressions were performed to evaluate the associations between each of the pre-operative KOOS and SF36 scores with knee pain at 7 years. Odd ratios for these measures were expressed per 10 unit decrease (greater severity) to represent a difference that is clinically meaningful.[9] Stepwise logistic regression was used to simultaneously evaluate baseline KOOS and SF36 scores as independent factors related to knee pain. To address the secondary hypothesis, the limb differences (surgical minus control limb) in the WORM and OARSI scores at 7 years were compared between the symptomatic and asymptomatic groups using Wilcoxon Sum Rank tests. The differences in joint space width (surgical minus control limb) between groups at 7 years were compared using an unpaired t-test. Analyses were performed using SAS statistical Software Version 9.4 (SAS Institute, Cary NC). Statistical significance was determined based on α=.05.

RESULTS

Patient Findings

Of the 90 subjects that formed the initial study cohort, the preoperative and postoperative questionnaires were completed by 72 subjects (80%) at 7 years. Onsight radiographic data were available for 59 subjects (66%) at 7 years. The mean patient age at the time of ACL reconstruction was 24 years (SD=8.8, range 15–47). Sixty and forty percent of subjects were female and male, respectively. The mean time from injury to surgery was 114 days (SD=79, range 9–364). Patellar tendon and four strand hamstring tendon autografts were used in 58 (63%) and 32 (37%) of the patients, respectively.

Symptomatic vs Asymptomatic Patients at 7 Years

Overall, a significant improvement was found between baseline and 7 year follow-up in all KOOS and SF36 component scores with the exception of SF36 general health (Table 1). Of the 72 subjects, 7 presented with KOOS pain scores 72 at 7 years and were categorized as symptomatic (Table 2). Significantly lower mean baseline scores were observed for symptomatic patients compared to asymptomatic patients on preoperative KOOS ADL

(12.6%, p=.023), KOOS Sports/Rec (24.9%, p=.004), KOOS Symptoms (13.8%, p=.046), SF36 Bodily Pain (9.0%, p=.004), SF36 Mental Health (16.72%, p=.009), and SF36 Physical Function (15.5%, p=.036). Unadjusted Odds ratios derived from logistic regression indicate that a 10 unit decrease in these measures at baseline was associated with increased odds of 45% to 79% for being classified as symptomatic at 7 years (KOOS ADL=71%, KOOS Sports/Rec=79%, KOOS Symptoms =59%, SF36 Bodily Pain=45%, SF36 Mental Health =72%, and SF36 Physical Function =50%.). When demographic and other baseline variables were examined, none were found to be significantly associated with symptomatic 7 year KOOS Pain score including sex (p=.95), age (p=.45), graft type (p=.61), initial graft tension (p=.23) and time to surgery (p=.36).

Multivariate Analysis for KOOS Pain at 7 years

Based on stepwise logistic regression, KOOS Sports/Rec and the SF36 Mental Health scores were found to be independently associated with the development of a symptomatic knee (Table 3). A 10 point decrease in baseline KOOS Sports/Rec increased the odds of having a symptomatic knee at 7 years by 82% while a corresponding decrease in SF36 Mental Health score increased the odds of having a symptomatic knee by 68% (Table 3).

Structural Changes Between Asymptomatic and Symptomatic Patients at 7 Years

At 7 years, the WORM score differences (surgical-contralateral control knee) between the symptomatic and asymptomatic subjects were significantly different (Table 4). The WORM score at 7 years was primarily driven by the presence of osteophytes (Supplemental Table S1). However, differences in the radiographic OARSI scores (p=.051) and medial joint space widths (p=.488) between the two groups were not significant at 7 years (Table 4). For reference, the means and standard deviations for the patient reported outcomes for both groups at 7 years are provided in Table 5. There were significant differences between the symptomatic and asymptomatic groups for all KOOS and 5 of the eight SF36 scores at 7 years.

DISCUSSION

The results of this study show that preoperatively administered patient reported outcome measures were associated with the development of a painful knee 7 years after ACL reconstruction. Specifically, the KOOS ADL, Sports/Recreation, and Symptoms scores were associated with post-operative knee pain in our univariate analysis. In addition, the SF36 Bodily Pain, Mental Health, and Physical Function domains were associated with worse outcomes. Using a multivariate logistic regression analysis, the KOOS Sports/Recreation and SF36 Mental Health scores were found to be significantly associated with the 7 year outcome. Specifically, for every 10 point decrease in the preoperative KOOS Sports/Recreation score, the odds of a symptomatic outcome as determined by KOOS Pain increased by 82%. For example, the mean pre-operative KOOS Sports/Recreation score of this ACL reconstruction cohort was 57.5. Therefore, a patient with a pre-operative KOOS Sports/Recreation score of 47.5 would be 82% more likely to have a KOOS pain score of 72 at 7 years when compared to a person with the mean score. Similarly, with every 10

point decrease in the SF36 Mental Health score, the odds of having an unacceptable pain outcome at 7 years increased by 68%.

Additionally, we showed MRI evidence of knee osteoarthritis in the symptomatic group. The significant difference in WORM scores between the operative knee and contralateral knee in the symptomatic group was 13.7 points compared to 5.8 in the asymptomatic group. The differences in OARSI radiographic scores between groups also approached significance (p=. 051). Both the WORM and OARSI scores were primarily driven by the presence of osteophytes (Supplemental Tables S1 & S2). These findings support that the KOOS Pain score identified symptoms associated with osteoarthritis. However, no differences were found between groups for medial joint space narrowing. The study may have been underpowered to identify this difference at this time point since a low percentage of the study subjects were symptomatic.

Prior studies have shown an association between ACL injury and the development of radiographic evidence of knee osteoarthritis.[1,24,26] Progression of knee osteoarthritis after ACL reconstruction has been shown to correlate with worse scores on most scores of the KOOS.[26] Several studies have examined preoperative and intra-operative factors associated with the development of symptoms of knee osteoarthritis following ACL reconstruction. [4–6,10,18,21,22,28,29] However, the majority of studies have focused on demographics and intraoperative findings often reporting conflicting results.[4] In the current study, we did not find any significant relationship between demographics or intraoperative findings and post-operative pain at 7 years.

Li et al.[21] retrospectively reviewed a cohort of 249 subjects at a median follow-up of 7.8 years and reported that 39% of the patients had radiographic evidence of osteoarthritis. They found prior medial meniscectomy, grade 2 or greater medial compartment chondral lesions, longer follow-up, and higher BMI to be associated with the development of osteoarthritis. However, the authors did not use patient reported outcome measures to determine which patients were symptomatic. Other authors have also shown an association between grade III/IV chondral lesions[10,18,28] or partial meniscectomy[6,18,29] and worse self-reported outcomes. In our study, subjects were excluded if they had an ICRS grade 2 or meniscal tears involving more than the central 1/3rd of the meniscus, which may have eliminated these variables as significant factors. While the exclusions of meniscal and chondral injuries from enrollment in the parent study[2,15] may limit generalizability these data provide insight into predicting outcomes following an isolated ACL injury.

Few studies have examined the effect of preoperative outcome scores on predicting post-operative outcomes. Spindler et al.[29] found that KOOS Sports/Recreation and KOOS QOL assessed at the time of surgery were associated with these same measures at 6 years following ACL reconstruction. Similarly, Dunn et al.[11] showed that the preoperative SF36 Mental Health score had the strongest relationship with post-operative SF36 Mental Health Score. However, to our knowledge, our study is the first to describe the association between baseline KOOS and SF36 scores in the development of a symptomatic knee at intermediate term (7 year) follow-up.

Our findings suggest that a low preoperative SF36 Mental Health score was associated with a symptomatic knee at 7 year follow-up. A low score on the SF36 Mental Health signifies feelings of nervousness and depression.[31] Recent literature has demonstrated a relationship between psychological factors and knee function and symptoms after ACL reconstruction. [14,16,20] Further study is warranted to investigate the relationship between preoperative SF-36 scores and other postoperative outcomes such as kinesiophobia and return to sports.

Our multivariate logistic regression model resulted in only two significant predictors, KOOS Sports/Recreation and SF36 Mental Health scores, both of which were highly significant in univariate analyses. Additionally, corresponding odds ratios for the multivariate analysis were very consistent with the univariate OR's (1.82 vs 1.79 and 1.68 vs 1.72) indicating that multicollinearity between explanatory variables did not impact the estimates. Nonetheless, the small sample size of the symptomatic group is a limitation of this study, which may not have been powered to detect other potentially relevant factors.

There are several other limitations to this study. Although the data were prospectively collected, the study was retrospective in that the research question was asked after the data were acquired. In addition, we selected the previously used cut-off of 72 for the KOOS Pain score to differentiate between a symptomatic and asymptomatic knee.[32] This value was derived from 2 standard deviations below the mean for a sample of subjects with a history of knee ligament injury.[32] However, there is currently no consensus on the best method for identifying patients with an unacceptable level of pain following ACL reconstruction. In addition, although other baseline measures, including age, weight, time to surgery, initial graft tension, chondral lesions, and meniscal lesions were not found to be associated with the KOOS Pain score at 7 years, the study may have been underpowered to detect these differences as only 7 of 72 patients met the criteria for symptomatic. However, the sample size was restricted to the number of patients originally enrolled in the base study.[15] Nonetheless, the follow-up at 7 years was 80%,[2] which is the accepted minimum standard follow-up rate for a Level 1 clinical trial. Despite the small sample size, we determined that both the pre-operative KOOS Sports/Recreation and SF36 Mental Health scores were associated with those patients that would present with a painful knee at 7 years.

In conclusion, preoperative KOOS and SF36 scores may provide insight for predicting intermediate term outcomes following ACL reconstruction. Specifically, the pre-operative KOOS Sports/Recreation and the SF36 Mental Health scores had the strongest association with future KOOS pain score 7 years following ACL reconstruction. In addition, worse outcomes, as determined by the KOOS Pain score, were associated with imaging evidence of knee osteoarthritis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Mean change in KOOS and SF36 scores between baseline and 7 years for all patients.

Outcome Measure	Baseline (Mean±SD)	7 Year (Mean ±SD)	Change (95% CI)	p-value
KOOS Pain [*]	77.0±15.6	91.9±17.3	18.9 (9.9–9.8)	<.001
KOOS ADL [*]	85.7±14.1	95.7±9.2	10.0 (6.5–3.5)	<.001
KOOS QOL [*]	37.6±18.2	78.6±21.5	41.0 (35.7–46.4)	<.001
KOOS Sports [*]	57.5±22.4	83.9±18.2	26.4 (20.7–32.0)	<.001
KOOS Symptoms [*]	71.1±17.4	84.1±16.0	13.0 (8.4–17.5)	<.001
SF36 BP [*]	62.7±16.4	81.7±16.2	19.0 (14.1–23.8)	<.001
SF36 GH	83.2±14.3	82.2±14.6	−1.0 (−5.1–3.1)	.636
SF36 MH [*]	73.7±16.4	82.4±13.8	8.8 (5.0–12.5)	.004
SF36 PF [*]	71.8±18.6	93.5± 9.9	21.7 (17.0–26.5)	<.001
SF36 RE [*]	86.0±20.9	95.3±11.6	9.3 (4.2–14.4)	<.001
SF36 RP [*]	60.6±26.0	95.9±10.2	35.3 (28.5–42.2)	<.001
SF36 SF [*]	80.4±19.4	93.2±14.1	12.8 (8.2–17.5)	<.001
SF36 V [*]	63.6±18.4	70.3±18.2	6.7 (1.5–11.8)	.012

[*] indicates a significant change from Baseline to 7 years based on paired t-test (p <.05).

KOOS = Knee Osteoarthritis Outcome Score; ADL = Activities of Daily Living; QOL = Knee Related Quality of Life; Sports = Sports & Recreation; BP = Bodily Pain; GH = General Health; MH = General Mental Health; PF = Limitations in Physical function; RE = limitations in usual role activities due to emotional problems; RP = limitations in usual role activities due to physical problems; SF = limitations in social activities due to physical or emotional problems; V = Vitality.

Table 2

Differences in baseline KOOS and SF36 scores between symptomatic and asymptomatic groups and the associated odds ratios. Odds-ratios represent the change in odds of being symptomatic per 10 unit decrease (i.e. representing an increase in severity) in the baseline measure.

Baseline Measure	Symptomatic Patients (n=7) Mean±SD	Asymptomatic Patients (n=65) Mean±SD	p-value	Odds Ratio	95% CI
KOOS Pain	68.7±16.1	77.9±15.4	.135	1.46	(0.88–2.42)
KOOS ADL *	74.4±19.9	86.9±12.8	.023	1.71	(1.04–2.81)
KOOS QOL	33.0±17.9	38.0±18.2	.487	1.18	(0.75–1.87)
KOOS Sports *	35.0±19.6	59.9±21.5	.004	1.79	(1.15–2.79)
KOOS Symptoms *	58.7±12.0	72.5±17.5	.046	1.59	(0.99–2.56)
SF36 BP *	54.6±5.1	63.6±17.0	.004	1.45	(0.84–2.51)
SF36 GH	83.6±11.2	83.2±14.7	.947	0.98	(0.56–1.71)
SF36 MH *	58.6±18.4	75.3±15.4	.009	1.72	(1.09–2.70)
SF36 PF *	57.9±18.7	73.3±18.1	.036	1.50	(1.01–2.25)
SF36 RE	83.7±19.3	86.3±21.2	.761	1.06	(0.74–1.50)
SF36 RP	45.5±26.5	62.2±25.6	.108	1.30	(0.93–1.82)
SF36 SF	73.2±18.3	81.1±19.5	.309	1.21	(0.83–1.77)
SF36 V	54.5±20.3	64.6±18.1	.167	1.31	(0.89–1.95)

*
indicates a significant difference between groups based on two-sample t-test (p<.05).

KOOS = Knee Osteoarthritis Outcome Score; ADL = Activities of Daily Living; QOL = Knee Related Quality of Life; Sports = Sports & Recreation; BP = Bodily Pain; GH = General Health; MH = General Mental Health; PF = Limitations in Physical function; RE = limitations in usual role activities due to emotional problems; RP = limitations in usual role activities due to physical problems; SF = limitations in social activities due to physical or emotional problems; V = Vitality.

Table 3

Significant findings from multivariate analysis assuming a 10 point change in the preoperative score.

Baseline Measure	Odds Ratio	95% CI	p-value
KOOS Sports	1.821	1.106–3.003	.005
SF36 MH	1.681	1.025–2.762	.025

KOOS = Knee Osteoarthritis Outcome Score; Sports = Sports & Recreation; MH = General Mental Health.

Table 4

Mean±SD for the imaging outcomes between the patients categorized as symptomatic compared to the asymptomatic patients using the KOOS pain score at 7 years. WORM Score Difference (Sx–Ctl), OARSI Xray Score Difference (Sx–Ctl) and Joint Space Width Difference (Sx–Ctl, mm). Sx = surgical knee; Ctl = contralateral control knee.

Outcome Measure	Symptomatic Patients (Mean±SD)	Asymptomatic Patients (Mean±SD)	p-value
WORM Score [*]	13.7±22.2	5.8±14.5	.047
OARSI Xray Score	2.8±5.0	0.8±1.9	.051
JSW (mm)	−0.32±0.68	−0.03±0.182	.487

[*] indicates a significant difference between groups.

OARSI = Osteoarthritis Research Society International; WORM = Whole Organ MRI; JSW = medial joint space width.

Table 5

Mean±SD for the patient reported outcomes at 7 years between the patients categorized as symptomatic compared to asymptomatic.

Outcome Measure	Symptomatic Patients (Mean±SD)	Asymptomatic Patients (Mean±SD)	p-value
KOOS Pain*	47.2±5.0	96.7±5.9	.002
KOOS ADL*	72.1±13.0	98.3±3.1	.002
KOOS QOL*	43.7±28.1	82.4±17.1	.010
KOOS Sports*	48.6±16.5	87.7±13.1	<.001
KOOS Symptoms*	53.5±15.5	87.4±12.1	<.001
SF36 BP*	54.4±14.3	84.6±13.4	<.001
SF36 GH*	65.2±15.0	84.1±13.4	<.001
SF36 MH	71.4±19.4	83.6±12.7	.025
SF36 PF*	75.0±15.3	95.5±6.7	.012
SF36 RE	84.5±21.7	96.5±9.5	.196
SF36 RP*	81.3±19.1	97.5±7.4	.065
SF36 SF*	73.2±22.2	95.4±11.2	.038
SF36 V	58.9±24.2	71.5±17.2	.081

*
indicates a significant difference between groups.

KOOS = Knee Osteoarthritis Outcome Score; ADL = Activities of Daily Living; QOL = Knee Related Quality of Life; Sports = Sports & Recreation; BP = Bodily Pain; GH = General Health; MH = General Mental Health; PF = Limitations in Physical function; RE = limitations in usual role activities due to emotional problems; RP = limitations in usual role activities due to physical problems; SF = limitations in social activities due to physical or emotional problems; V = Vitality. Significance determined by 2-sample t-test.